D. Qiang
523455

=> fil medl,caplus,biosis,embase,wpids,scisearch,ntis,jicst

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=> s (infertil? or steril? or unproduct? or fertil?) and (control? ovar? stimulat? or cos) and (assist? reproduc? proced? or art)

L1	1	FILE MEDLINE
L2	2	FILE CAPLUS
L3	1	FILE BIOSIS
L4	1	FILE EMBASE
L5	3	FILE WPIDS
L6	1	FILE SCISEARCH
L7	0	FILE NTIS
L8	0	FILE JICST-EPLUS

TOTAL FOR ALL FILES
L9 9 (INFERTIL? OR STERIL? OR UNPRODUCT? OR FERTIL?) AND (CONTROL? OVAR? STIMULAT? OR COS) AND (ASSIST? REPRODUC? PROCED? OR ART)

=> dup rem l9

PROCESSING COMPLETED FOR L9
L10 7 DUP REM L9 (2 DUPLICATES REMOVED)

=> d cbib abs 1-7;s (suppress?(1)prematur? ovulat? or ovar? fail?(a)prematur?) and (lhrh or leuteiniz? hormone releas? hormone or gonadorelin or gonadoliberin or lh releas? hormone or luliberin or fsh releas? hormone or follicle stimulat?)

L10 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1
2000:725497 Document No. 133:261948 Method for a programmed **controlled ovarian stimulation** protocol.
Engel, Jurgen; Riethmuller-winzen, Hilde (Asta Medica A.-G., Germany). PCT Int. Appl. WO 2000059542 A1 20001012, 17 pp. DESIGNATED STATES: W: AU, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 2000-EP2466 20000321. PRIORITY: US 1999-PV127241 19990331; US 1999-PV131632 19990428.

AB A method of therapeutic management of **infertility** by programming of **controlled ovarian stimulation** (**COS**) and **assisted reproductive procedures** (**ART**) the improvement consisting of (a) suppression of premature ovulation with an LHRH-antagonist in **controlled ovarian stimulation** (**COS**) and assisted reproductive techniques (**ART**) with multiple follicle and oocyte development; (b) programming the start of **controlled ovarian stimulation** (**COS**) by the administration of progestogen only - or alternatively combined oral contraceptive prepns.; (c) exogenous stimulation of the ovarian follicle growth; (d) ovulation induction with HCG, native LHRH, LHRH-agonists or recombinant LH; (e) application of assisted reprodn. techniques, esp. of IVF, ICSI, GIFT, ZIFT or by intrauterine insemination by sperm injection.

L10 ANSWER 2 OF 7 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-376519 [32] WPIDS
AB WO 200027997 A UPAB: 20000706
NOVELTY - A method for obtaining human erythropoietin (EPO) from recombinant mammalian cells is new and the culture medium comprises insulin.

USE - The method is used for the production of human erythropoietin (EPO) on a large scale. The EPO is then used for a variety of purposes (not defined).

ADVANTAGE - The present invention allows erythropoietin to be produced on an industrial scale, and overcomes the problems of low reproducibility and output quality inherent with prior **art** method.

Dwg.0/4

L10 ANSWER 3 OF 7 SCISEARCH COPYRIGHT 2001 ISI (R)
2000:523719 The Genuine Article (R) Number: 330GH. Four-neutrino oscillation solutions of the solar neutrino problem - **art**. no. 013005.
Giunti C (Reprint); GonzalezGarcia M C; PenaGaray C. UNIV TURIN, IST NAZL FIS NUCL, SEZ TORINO, I-10125 TURIN, ITALY (Reprint); UNIV TURIN, DIPARTMENTO FIS TEOR, I-10125 TURIN, ITALY; UNIV VALENCIA, CSIC, INST FIS CORPUSCULAR, EDIFICIO INST PATERNA, VALENCIA 46071, SPAIN. PHYSICAL REVIEW D (1 JUL 2000) Vol. 6201, No. 1, pp. 3005-&. Publisher: AMERICAN PHYSICAL SOC. ONE PHYSICS ELLIPSE, COLLEGE PK, MD 20740-3844. ISSN: 0556-2821. Pub. country: ITALY; SPAIN. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We present an analysis of the neutrino oscillation solutions of the solar neutrino problem in the framework of four-neutrino mixing where a **sterile** neutrino is added to the three standard ones. We perform a nt to the full data set corresponding to the 825-day Super-Kamiokande data sample as well as to chlorine, GALLEX, and SAGE and Kamiokande experiments. In our analysis we use all measured total event rates as well as all Super-Kamiokande data on the zenith angle dependence and the recoil electron energy spectrum. We consider both transitions via the Mikheyev-Smirnov-Wolfenstein (MSW) mechanism as well as oscillations in vacuum (just-so) and find the allowed solutions for different values of the additional mixing angles. This framework permits transitions into active or **sterile** neutrinos controlled by the additional parameter **cos**(2)(theta(23))**cos**(2)(theta(24)) and contains as limiting cases the pure nu(e)-active and nu(e)-**sterile** neutrino oscillations. We discuss the maximum allowed values of this additional mixing parameter for the different solutions. As a particularity, we also show that for MSW transitions there are solutions at 99% C.L. at theta(12) mixing angles greater than pi/4 and that the best-fit point for the zenith angle distribution is in the second octant.

L10 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2001 ACS

2000:788971 Document No. 134:80871 LH-RH analogues: I. Their impact on reproductive medicine. Schally, Andrew V. (Endocrine, Polypeptide and Cancer Institute, Veterans Affairs Medical Center, and Department of Medicine, Tulane University School of Medicine, New Orleans, LA, 70112-2699, USA). Int. Congr. Ser., 1206(Current Knowledge in Reproductive Medicine), 183-194 (English) 2000. CODEN: EXMDA4. ISSN: 0531-5131. Publisher: Elsevier Science B.V..

AB A review, with 81 refs. In the 29 yr that have passed since the elucidation of the structure of LH-RH, diverse clin. applications in the field of reproductive medicine and related fields have been established for agonists of LH-RH, based on inhibition of the pituitary-gonadal axis. Various clin. investigations with agonists of LH-RH in benign gynecol. disorders, PCOD, IVF-ET, BPH, precocious puberty and contraception were reviewed. LH-RH antagonists inhibit LH, FSH, and sex steroid secretion immediately after the administration and thus, achieve rapid therapeutic effects. LH-RH antagonists should find applications in the treatment of uterine leiomyomas, endometriosis, and in **controlled ovarian stimulation**-assisted reproductive techniques (**COS-ART**), which have been already established for the agonists. Modern LH-RH antagonists such as Cetrorelix may prove superior to the agonists in **COS-ART** and also in the treatment of BPH, but addnl. studies in these and other areas are needed.

L10 ANSWER 5 OF 7 BIOSIS COPYRIGHT 2001 BIOSIS

2000:457318 Document No.: PREV200000457318. Predictive value of day 3 menstrual cycle FSH in young women (<35 years) undergoing assisted reproduction treatment (**ART**. Jacob, S. (1); Conroy, R.; Harrison, R. F. (1). (1) Human Assisted Reproduction Ireland, Rotunda Hospital, Royal College of Surgeons in Ireland, Dublin 2 Ireland. Human Reproduction (Oxford), (June, 2000) Vol. 15, No. Abstract Book 1, pp. 23. print. Meeting Info.: 16th Annual Meeting of the European Society of Human

Reproduction and Embryology Bologna, Italy June 25-28, 2000 European Society of Human Reproduction and Embryology. ISSN: 0268-1161. Language: English. Summary Language: English.

L10 ANSWER 6 OF 7 MEDLINE DUPLICATE 2
2000149595 Document Number: 20149595. LH-RH analogues: I. Their impact on reproductive medicine. Schally A V. (Endocrine, Polypeptide and Cancer Institute, Veterans Affairs Medical Center, New Orleans, Louisiana 70112-1262, USA.) GYNECOLOGICAL ENDOCRINOLOGY, (1999 Dec) 13 (6) 401-9. Ref: 81. Journal code: 125. ISSN: 0951-3590. Pub. country: ENGLAND: United Kingdom. Language: English.

AB In the 28 years that have passed since the elucidation of the structure of luteinizing hormone-releasing hormone (LH-RH), diverse clinical applications in the field of reproductive medicine and related fields have been established for agonists of LH-RH, based on inhibition of the pituitary-gonadal axis. Various clinical investigations with agonists of LH-RH in benign gynecologic disorders, polycystic ovary disease (PCOD), in vitro **fertilization**-embryo transfer (IVF-ET), benign prostatic hypertrophy (BPH), precocious puberty and contraception were reviewed. LH-RH antagonists inhibit LH, follicle-stimulating hormone (FSH), and sex steroid secretion immediately after their administration and thus achieve rapid therapeutic effects. LH-RH antagonists should find applications in the treatment of uterine leiomyomas, endometriosis, and in **controlled ovarian stimulation**-assisted reproductive techniques (**COS-ART**), which have been already established for the agonists. Modern LH-RH antagonists such as cetrorelix may prove superior to the agonists in **COS-ART** and also in the treatment of BPH, but additional studies in these and other areas are needed.

L10 ANSWER 7 OF 7 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-106510 [10] WPIDS
AB CA 2200541 A UPAB: 19990310
A method for treating **infertility** disorders by administering a luteinising hormone-releasing hormone (LH-RH) antagonist and inducing follicle growth by administration of exogenous gonadotropin, comprises the additional improvement of administering LH-RH antagonist at an amount which selectively suppresses endogenous LH but not follicle stimulating hormone (FSH) secretion, which retained at a natural level thus not affecting the individuals oestrogen levels.

ADVANTAGE - The method provides a **controlled ovarian stimulation**, while avoiding hyperstimulation syndrome as experienced by prior **art** methods.

Dwg.0/0

L11 95 FILE MEDLINE
L12 14 FILE CAPLUS
L13 58 FILE BIOSIS
L14 99 FILE EMBASE

```
L15           1 FILE WPIDS
L16          87 FILE SCISEARCH
L17           1 FILE NTIS
L18           2 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L19         357 (SUPPRESS?(L) PREMATUR? OVULAT? OR OVAR? FAIL?(A) PREMATUR?)
                AND (LHRH OR LEUTEINIZ? HORMONE RELEAS? HORMONE OR GONADORELIN
                OR GONADOLIBERIN OR LH RELEAS? HORMONE OR LULIBERIN OR FSH
RELEA
                S? HORMONE OR FOLLICLE STIMULAT?)

=> s (gonadotropin resist? ovar? syndrome or resist? ovar? syndrome) and
(lhrh or leuteiniz? hormone releas? hormone or gonadorelin or gonadoliberin
or lh releas? hormone or luliberin or fsh releas? hormone or follicle
stimulat?)

L20          11 FILE MEDLINE
L21           1 FILE CAPLUS
L22           9 FILE BIOSIS
L23          14 FILE EMBASE
L24           0 FILE WPIDS
L25           2 FILE SCISEARCH
L26           0 FILE NTIS
L27           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L28          37 (GONADOTROPIN RESIST? OVAR? SYNDROME OR RESIST? OVAR?
SYNDROME)
                AND (LHRH OR LEUTEINIZ? HORMONE RELEAS? HORMONE OR GONADORELIN
                OR GONADOLIBERIN OR LH RELEAS? HORMONE OR LULIBERIN OR FSH
RELEA
                S? HORMONE OR FOLLICLE STIMULAT?)

=> s (l28 or l19) and (control? ovar? stimulat? or cos or assist? reproduc?
technique? or "art" or progestogen or progestat? hormone?)

L29           3 FILE MEDLINE
L30           2 FILE CAPLUS
L31           1 FILE BIOSIS
L32           2 FILE EMBASE
L33           1 FILE WPIDS
L34           2 FILE SCISEARCH
L35           0 FILE NTIS
L36           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L37          11 (L28 OR L19) AND (CONTROL? OVAR? STIMULAT? OR COS OR ASSIST?
                REPRODUC? TECHNIQUE? OR "ART" OR PROGESTOGEN OR PROGESTAT?
HORMO
                NE?)

=> s l37 and (icsi or sperm inject(a)intracytoplasmic or hcg or human
chorionic gonadotropin or zift or zygote intrafallopian transfer or gift or
gamete intrafallopian transfer)
```

L38 0 FILE MEDLINE
L39 1 FILE CAPLUS
L40 0 FILE BIOSIS
L41 1 FILE EMBASE
L42 1 FILE WPIDS
L43 0 FILE SCISEARCH
L44 0 FILE NTIS
L45 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L46 3 L37 AND (ICSI OR SPERM INJECT(A) INTRACYTOPLASMIC OR HCG OR HUMAN CHORIONIC GONADOTROPIN OR ZIFT OR ZYGOTE INTRAFALLOPIAN TRANSFER OR GIFT OR GAMETE INTRAFALLOPIAN TRANSFER)

=> dup rem l46

PROCESSING COMPLETED FOR L46
L47 2 DUP REM L46 (1 DUPLICATE REMOVED)

=> d cbib abs

L47 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1
2000:725497 Document No. 133:261948 Method for a programmed **controlled ovarian stimulation** protocol.
Engel, Jurgen; Riethmuller-winzen, Hilde (Asta Medica A.-G., Germany).
PCT Int. Appl. WO 2000059542 A1 20001012, 17 pp. DESIGNATED STATES: W: AU, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2.
APPLICATION: WO 2000-EP2466 20000321. PRIORITY: US 1999-PV127241 19990331; US 1999-PV131632 19990428.
AB A method of therapeutic management of infertility by programming of **controlled ovarian stimulation** (**COS**) and assisted reproductive procedures (**ART**) the improvement consisting of (a) **suppression** of **premature ovulation** with an **LHRH**-antagonist in **controlled ovarian stimulation** (**COS**) and **assisted reproductive techniques** (**ART**) with multiple follicle and oocyte development; (b) programming the start of **controlled ovarian stimulation** (**COS**) by the administration of **progestogen** only - or alternatively combined oral contraceptive prepns.; (c) exogenous stimulation of the ovarian follicle growth; (d) ovulation induction with **HCG**, native **LHRH**, **LHRH**-agonists or recombinant LH; (e) application of **assisted reprodn. techniques**, esp. of IVF, **ICSI**, **GIFT**, **ZIFT** or by intrauterine insemination by sperm injection.

=> d cbib abs 2

L47 ANSWER 2 OF 2 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
94192356 EMBASE Document No.: 1994192356. **Premature ovarian**

failure. Davis A.P.. Dept of Obstetrics and Gynaecology, University Hospital of Wales,Heath Park, Cardiff CF4 4XW, United Kingdom. Contemporary Reviews in Obstetrics and Gynaecology 6/2 (95-99) 1994. ISSN: 0953-9182. CODEN: CROGEV. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB **Premature ovarian failure**, as diagnosed on finding raised FSH and LH levels and a low oestrogen concentration, encompasses a variety of different conditions. Some, but not all, are associated with an irreversible loss of ovarian function. This is determined by the presence or absence of ovarian follicles. Follicular forms of **premature ovarian failure** are found in the **resistant ovary syndrome** and in early stage autoimmune oophoritis. Afollicular forms exist in association with X-chromosome abnormalities (e.g. Turner's mosaicism), end-stage autoimmune oophoritis and with a true premature menopause. In the case of autoimmune oophoritis, treatment early in the disease may halt or reverse ovarian damage. The patient should also be screened for other autoimmune conditions, which can then be appropriately treated. If a woman is complaining of infertility, efforts should be directed towards making a specific diagnosis of the underlying condition. This may involve an ovarian biopsy, obtained either through the laparoscope or by performing a mini-laparotomy. If follicles are found, there is a 30 per cent spontaneous recovery rate in women with **resistant ovary syndrome**. Current methods to stimulate ovulation are probably no more successful, but should be offered when the secondary amenorrhoea has been prolonged or when oocyte donation is unacceptable to the couple and in vitro fertilization facilities are unavailable. In vitro fertilization and **gamete intrafallopian transfer** with hormonal manipulation are the most successful **assisted reproduction techniques** for this condition. Afollicular women wishing to conceive should also be offered these techniques. All women with **premature ovarian failure** should be offered hormone replacement therapy.

```
=> s engel j?/au,in

'IN' IS NOT A VALID FIELD CODE
L48        1088 FILE MEDLINE
L49        1239 FILE CAPLUS
L50        1595 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L51        1015 FILE EMBASE
L52         285 FILE WPIDS
'IN' IS NOT A VALID FIELD CODE
L53        1730 FILE SCISEARCH
'IN' IS NOT A VALID FIELD CODE
L54           0 FILE NTIS
L55          18 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L56        6970 ENGEL J?/AU,IN

=> s l56 and (infertil? or steril? or fertil?)
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```
L57            5 FILE MEDLINE
L58           12 FILE CAPLUS
L59            6 FILE BIOSIS
L60            7 FILE EMBASE
L61            8 FILE WPIDS
L62            4 FILE SCISEARCH
L63            0 FILE NTIS
L64            0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L65           42 L56 AND (INFERTIL? OR STERIL? OR FERTIL?)

=> s l37 not l46;s l65 not (l9 or l46)

L66            3 FILE MEDLINE
L67            1 FILE CAPLUS
L68            1 FILE BIOSIS
L69            1 FILE EMBASE
L70            0 FILE WPIDS
L71            2 FILE SCISEARCH
L72            0 FILE NTIS
L73            0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L74            8 L37 NOT L46


L75            5 FILE MEDLINE
L76           11 FILE CAPLUS
L77            6 FILE BIOSIS
L78            7 FILE EMBASE
L79            6 FILE WPIDS
L80            4 FILE SCISEARCH
L81            0 FILE NTIS
L82            0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L83           39 L65 NOT (L9 OR L46)

=> s l83 not l74

L84            5 FILE MEDLINE
L85           11 FILE CAPLUS
L86            6 FILE BIOSIS
L87            7 FILE EMBASE
L88            6 FILE WPIDS
L89            4 FILE SCISEARCH
L90            0 FILE NTIS
L91            0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L92           39 L83 NOT L74

=> dup rem l74
```

PROCESSING COMPLETED FOR L74
L93 4 DUP REM L74 (4 DUPLICATES REMOVED)

=> d 1-4 cbib abs;dup rem 192

L93 ANSWER 1 OF 4 MEDLINE DUPLICATE 1
2000173931 Document Number: 20173931. Pharmacokinetic-pharmacodynamic modeling of testosterone and luteinizing hormone suppression by cetrorelix in healthy volunteers. Pechstein B; Nagaraja N V; Hermann R; Romeis P; Locher M; Derendorf H. (Department of Biological Research Biochemistry, ASTA Medica AG, Frankfurt, Germany.) JOURNAL OF CLINICAL PHARMACOLOGY, (2000 Mar) 40 (3) 266-74. Journal code: HT9. ISSN: 0091-2700. Pub. country: United States. Language: English.

AB Cetrorelix (CET), a potent luteinizing hormone-releasing hormone (LH-RH) antagonist, was recently approved for the prevention of **premature ovulation** in patients undergoing a **controlled ovarian stimulation** (**COS**), followed by oocyte pickup and **assisted reproductive techniques** (**ART**), and is currently under clinical trials for benign prostate hyperplasia, endometriosis, and tumors sensitive to sex hormones.

CET **suppresses** luteinizing hormone (LH), **follicle-stimulating** hormone (FSH), and testosterone (T) in men. The purpose of this study was to evaluate the pharmacokinetics and absolute bioavailability of 3 mg intravenously and subcutaneously administered CET in healthy male and female volunteers and to develop a pharmacokinetic-pharmacodynamic (PK-PD) model to link the plasma concentrations of CET to the T and LH **suppression** in males. Following intravenous (IV) (n = 5) and subcutaneous (SC) (n = 6) administration of CET acetate, CET and hormone plasma levels were measured by radioimmunoassay (RIA) and enzyme immunoassay (EIA) methods, respectively. Pharmacokinetics of CET was explained by a three-compartment model for the IV route and by a two-compartment model with first-order absorption for the SC route. Average absolute bioavailability after SC administration was 85%. There were no differences in the pharmacokinetics between male and female subjects (ANOVA, $p > 0.05$). Single IV and SC doses of CET caused immediate and distinct **suppression** of LH, FSH, and T levels by 80%, 45% and 95% of their baseline levels, respectively. The duration of hormone **suppression** was longer for the SC route. An indirect-response PK-PD Emax model was developed to link the measured CET plasma concentrations with the respective T or LH levels. In addition, the circadian rhythm of T levels was accounted by including a cosine function in a second separate PD model. The PD model with cosine function was applied to T baseline levels as well as to the **suppressed** concentrations after CET dosing. The two models adequately described the PK-PD relationship between plasma levels of CET and T **suppression** following IV and SC dosing. The EC50 values (mean +/- SD) for the **suppression** of T were similar ($p > 0.05$) between the two routes of administration and the two models.

L93 ANSWER 2 OF 4 MEDLINE
2000017940 Document Number: 20017940. New natural inactivating mutations of the **follicle-stimulating** hormone receptor: correlations between receptor function and phenotype. Touraine P; Beau I; Gougeon A; Meduri G; Desroches A; Pichard C; Detoeuf M; Paniel B; Prieur M; Zorn J R; Milgrom E; Kuttenn F; Misrahi M. (Department of Endocrinology and Reproductive Medicine, Hopital Necker, Institut Federatif de Recherche (IFR-NEM), Paris, France.) MOLECULAR ENDOCRINOLOGY, (1999 Nov) 13 (11) 1844-54. Journal code: NGZ. ISSN: 0888-8809. Pub. country: United States.
Language: English.
AB **Premature ovarian failure** occurs in almost 1% of women under age 40. Molecular alterations of the FSH receptor (FSHR) have recently been described. A first homozygous mutation of the FSHR was identified in Finland. More recently, we described two new mutations of the FSHR in a woman presenting a partial FSH-resistance syndrome (patient 1). We now report new molecular alterations of the FSHR in another woman (patient 2) who presented at the age of 19 with primary amenorrhea contrasting with normal pubertal development. She had high plasma FSH, and numerous ovarian follicles up to 3 mm in size were evidenced by ultrasonography. Histological and immunohistochemical examination of ovarian biopsies revealed the presence of a normal follicular development up to the antral stage and disruption at further stages. DNA sequencing showed two heterozygous mutations: Asp224Val in the extracellular domain and Leu601Val in the third extracellular loop of FSHR. Cells transfected with expression vectors encoding the wild type or the mutated Leu601Val receptors bound hormone with similar affinity, whereas binding was barely detectable with the Asp224Val mutant. Confocal microscopy showed the latter to have an impaired targeting to the cell membrane. This was confirmed by its accumulation as a mannose-rich precursor. Adenylate cyclase stimulation by FSH of the Leu601Val mutant receptor showed a 12+/-3% residual activity, whereas in patient 1 a 24+/-4% residual activity was detected for the Arg573Cys mutant receptor. These results are in keeping with the fact that estradiol and inhibin B levels were higher in patient 1 and that stimulation with recombinant FSH did not increase follicular size, estradiol, or inhibin B levels in patient 2 in contrast to what was observed for patient 1. Thus, differences in the residual activity of mutated FSHR led to differences in the clinical, biological, and histological phenotypes of the patient.

L93 ANSWER 3 OF 4 MEDLINE DUPLICATE 2
2000022411 Document Number: 20022411. Preservation of fertility and ovarian function and minimizing chemotherapy-induced gonadotoxicity in young women. Blumenfeld Z; Avivi I; Ritter M; Rowe J M. (Department of Obstetrics and Gynecology, Rambam Medical Center, Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel.. bzeev@techunix.technion.ac.il) . JOURNAL OF THE SOCIETY FOR GYNECOLOGIC INVESTIGATION, (1999 Sep-Oct) 6 (5) 229-39. Ref: 125. Journal code: CMH. ISSN: 1071-5576. Pub. country: United States. Language: English.
AB BACKGROUND: After the improved long-term survival in young women with lymphoma and leukemia undergoing chemotherapy, the preservation of future

fertility has been the focus of recent interest. AREAS OF REVIEW: Three major topics are reviewed. They include the following: (1) the role of chemotherapy in the treatment of malignant and nonmalignant disease in young women, the types of chemotherapy and their gonadal effects (differing between ovaries and testes) in both human and other species, and the reasons for differences in the outcomes of various studies; (2) the human experience with GnRH-agonist therapy for minimizing chemotherapy-associated gonadotoxicity; and (3) inhibin measurements in young women treated by chemotherapy and in perimenopausal patients and those with impending **premature ovarian failure** (POF). Whereas egg retrieval for in vitro fertilization (IVF) and embryo cryopreservation is a valid assisted reproductive technology (**ART**) for married couples, it may be unacceptable for the young single woman. The investigational endeavors of ovarian cryopreservation awaits the clinical experience of in vitro maturation of thawed primordial follicles, their IVF, and embryo transfer. Although promising, this experience is not yet available. Moreover, the risk of possible reimplantation of malignant stem cells with the thawed cryopreserved ovary has been raised after animal observations. Therefore, until these innovative endeavors prove successful, and in parallel with them, an attempt was made to minimize the gonadotoxic effect of chemotherapy by the cotreatment with a GnRH agonistic analogue (GnRH-a) to induce a temporary prepubertal milieu, because prepubertal ovaries were found more resistant to alkylating agents' effect than the ovaries of older women. To characterize the correlation with ovarian function after gonadotoxic chemotherapy for Hodgkin or non-Hodgkin lymphoma in young women, the immunoreactive inhibin-A concentrations in the sera of these patients were measured before, during, and after the gonadotoxic chemotherapy. CONCLUSIONS: The GnRH-a cotreatment should be considered in every woman in the reproductive age receiving chemotherapy, in addition to **ART** and the investigational attempts of ovarian cryopreservation for future in vitro maturation or reimplantation. If these preliminary data are confirmed in a larger group of patients, inhibin-A concentrations may serve as a prognostic factor for predicting the resumption of ovarian function in addition to the levels of FSH, LH, and estradiol.

L93 ANSWER 4 OF 4 SCISEARCH COPYRIGHT 2001 ISI (R)

1998:800479 The Genuine Article (R) Number: 127ZE. A novel phenotype related to partial loss of function mutations of the **follicle stimulating** hormone receptor. Beau I; Touraine P; Meduri G; Gougeon A; Desroches A; Matuchansky C; Milgrom E; Kuttenn F; Misrahi M (Reprint). HOP BICETRE, INSERM, U135, 3EME NIVEAU, 78 RUE GEN LECLERC, F-94275 LE KREMLIN BICETR, FRANCE (Reprint); HOP BICETRE, INSERM, U135, F-94275 LE KREMLIN BICETR, FRANCE; HOP BICETRE, LAB HORMONOL & BIOL MOL, ASSISTANCE PUBL HOP PARIS, F-94275 LE KREMLIN BICETR, FRANCE; INST FED RECH 21, F-94275 LE KREMLIN BICETR, FRANCE; HOP NECKER ENFANTS MALAD, SERV ENDOCRINOL & MED REPROD, F-75743 PARIS 15, FRANCE; FAC MED LYON SUD, INSERM, U407, F-69600 OULLINS, FRANCE. JOURNAL OF CLINICAL INVESTIGATION (1 OCT 1998) Vol. 102, No. 7, pp. 1352-1359. Publisher: ROCKEFELLER UNIV PRESS. 1114 FIRST AVE, 4TH FL, NEW YORK, NY 10021. ISSN: 0021-9738. Pub.

country: FRANCE. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB A single natural loss of function mutation of the **follicle stimulating** hormone receptor (FSHR) has been described to date. Present in the Finnish population it markedly impairs receptor function, blocking follicle development at the primary stage and presenting as primary amenorrhea with atrophic ovaries. When Western European women with this phenotype were examined for FSHR mutations the result was negative, suggesting that other etiologies corresponding to this clinical pattern are markedly more frequent.

We now describe a novel phenotype related to mutations provoking a partial loss of function of the FSHR. A woman with secondary amenorrhea had very high plasma gonadotropin concentrations (especially FSH), contrasting with normal sized ovaries and antral follicles up to 5 mm at ultrasonography. Histological and immunohistochemical examination of the ovaries showed normal follicular development up to the small antral stage and a disruption at further stages. The patient was found to carry compound heterozygotic mutations of the FSHR gene: Ile160Thr and Arg573Cys substitutions located, respectively, in the extracellular domain and in the third intracellular loop of the receptor. The mutated receptors, when expressed in **COS**-7 cells, showed partial functional impairment, consistent with the clinical and histological observations: the first mutation impaired cell surface expression and the second altered signal transduction of the receptor.

This observation suggests that a limited FSH effect is sufficient to promote follicular growth up to the small antral stage. Further development necessitates strong FSH stimulation. The contrast between very high FSK levels and normal sized ovaries with antral follicles may thus be characteristic of such patients.

PROCESSING COMPLETED FOR L92
L94 22 DUP REM L92 (17 DUPLICATES REMOVED)

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L94 ANSWER 1 OF 22 MEDLINE DUPLICATE 1
2000153527 Document Number: 20153527. Ovarian stimulation with HMG: results of a prospective randomized phase III European study comparing the luteinizing hormone-releasing hormone (LHRH)-antagonist cetrorelix and the LHRH-agonist buserelin. European Cetrorelix Study Group. Albano C; Felberbaum R E; Smitz J; Riethmuller-Winzen H; **Engel J**; Diedrich K; Devroey P. (Centre for Reproductive Medicine, Dutch-speaking Brussels Free University, Belgium.) HUMAN REPRODUCTION, (2000 Mar) 15 (3) 526-31. Journal code: HRP. ISSN: 0268-1161. Pub. country: ENGLAND: United Kingdom.
Language: English.
AB In this prospective and randomized study, 188 patients received the luteinizing hormone-releasing hormone (LHRH) antagonist cetrorelix, and

patients the LHRH agonist buserelin to prevent endogenous luteinizing hormone (LH) surges during ovarian stimulation in in-vitro **fertilization** (IVF)/intracytoplasmic sperm injection (ICSI) cycles. Ultimately, 181 patients (96.3%) in the cetrorelix group, and 77 (90.6%) in the buserelin group, reached the day of the human chorionic gonadotrophin (HCG) injection. The mean number of human menopausal gonadotrophin (HMG) ampoules administered and the mean number of stimulation days with HMG were significantly less in the cetrorelix group than in the buserelin group ($P < 0.01$). A rise in LH and progesterone concentrations was observed in three of the 188 patients (1.6%) who received cetrorelix. On the day of the HCG administration, more follicles of a small diameter (11-14 mm) were observed in the buserelin group than in the cetrorelix group ($P = 0.02$) and the mean serum oestradiol concentration was significantly higher in patients who received buserelin than in those who received cetrorelix ($P < 0.01$). Similar results were observed in **fertilization**, cleavage and pregnancy rates in the two groups. In conclusion, the use of the LHRH antagonists might be considered more advantageous because of the short-term application needed to inhibit gonadotrophin secretion, so allowing a reduction in the treatment time in a clinically significant manner.

L94 ANSWER 2 OF 22 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 2
2000:422382 Document No.: PREV200000422382. The LHRH antagonist Cetrorelix: A review. Reissmann, T. (1); Schally, A. V.; Bouchard, P.; Riethmueller, H.;
Engel, J.. (1) Corporate Research and Development, ASTA Medica AG, Weismuellerstrasse 45, D-60314, Frankfurt Germany. Human Reproduction Update, (July August, 2000) Vol. 6, No. 4, pp. 322-331. print. ISSN: 1355-4786. Language: English. Summary Language: English.
AB In those clinical situations in which an immediate and profound suppression of gonadotrophins is desired, LHRH agonists have the disadvantage of producing an initial stimulatory effect on hormone secretion. Therefore, the use of GnRH antagonists which cause an immediate and dose-related inhibition of LH and FSH by competitive blockade of the receptors is much more advantageous. One of the most advanced antagonist produced to date is Cetrorelix, a decapeptide which has been shown to be safe and effective in inhibiting LH and sex-steroid secretion in a variety of animal species and in clinical studies as well. Clinical trials in patients suffering from advanced carcinoma of the prostate, benign prostate hyperplasia, and ovarian cancer are currently in progress and have already shown the usefulness of this new treatment modality. In particular, the concept that a complete suppression of sex-steroids may not be necessary in indications such as uterine fibroma, endometriosis and benign prostatic hyperplasia represents a promising novel perspective for treatment of these diseases. Following completion of phase III trials in controlled ovarian stimulation for IVF regimens, Cetrorelix was given marketing approval and, thus, became the first LHRH antagonist available clinically.

L94 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 3
1999:708625 Document No. 131:295922 Method for the treatment of **fertility** disorders using an LHRH antagonist to partially suppress endogenous gonadotropins during intrauterine insemination. **Engel,**

Jurgen; Riethmuller-Winzen, Hilde; Reissmann, Thomas (Asta Medica Aktiengesellschaft, Germany). PCT Int. Appl. WO 9955357 A1 19991104, 13 pp. DESIGNATED STATES: W: AU, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1999-EP2133 19990329. PRIORITY: US 1998-82743 19980423.

AB In the method of therapeutic management of **infertility** by intrauterine insemination the improvement consisting of (a) the dose-dependent suppression of endogenous gonadotropins, esp. LH, with a LH-RH Antagonist allowing the maintenance of physiol. estrogen levels, (b) exogenous stimulation of the ovarian follicle growth, (c) ovulation induction with HCG, native LHRH, LHRH-Agonists or recombinant LH, (d) intrauterine insemination by sperm injection. The LHRH Antagonists may be preferably Cetrorelix or Antarelix. The stimulation is performed by administration of HMG or recombinant FSH with or without recombinant LH or with antiestrogens as for example Chlomiphene as well as with the combination of antiestrogens as for example Chlomiphene with gonadotropins.

L94 ANSWER 4 OF 22 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-542841 [46] WPIDS
CR 1994-265229 [33]
AB EP 947200 A UPAB: 19991110
NOVELTY - **Sterile** freeze-dried cetrorelix acetate (a peptide described in EP299402) is used in the treatment of female **infertility**.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) use of **sterile** freeze-dried cetrorelix acetate for protecting gonads against noxious agents that damage germ cells, e.g. radiation treatment and chemotherapy; (2) a composition comprising **sterile** freeze-dried cetrorelix acetate and optionally excipients for use in the treatment of female **infertility**; (3) a composition comprising **sterile** freeze-dried cetrorelix acetate and optionally excipients for protecting gonads against noxious agents that damage germ cells, e.g. radiation treatment and chemotherapy with cytostatic agents.

ACTIVITY - None given.

MECHANISM OF ACTION - Luteinizing hormone-releasing hormone (LHRH) antagonist.

USE - In an in-vitro **fertilization** procedure in which cetrorelix is administered to control the time of ovulation during an ovary stimulation treatment by preventing a pre-ovulation increase in luteinizing hormone (LH) levels, whereupon exogenous gonadotropin is administered to induce ovulation after follicle maturation.
Dwg.0/0

L94 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2001 ACS
1998:672495 Document No. 129:293891 Immobilized activity-stabilized LHRH antagonist complexes and their production. **Engel, Juergen**; Deger, Wolfgang; Reissmann, Thomas; Losse, Guenter; Naumann, Wolfgang; Murgas, Sandra (Asta Medica Aktiengesellschaft, Germany). PCT Int. Appl.

WO 9842381 A1 19981001, 22 pp. DESIGNATED STATES: W: AU, BR, CA, CN, CZ, HU, IL, JP, MX, NO, NZ, PL, RU, SK, TR, UA; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (German). CODEN: PIXXD2. APPLICATION: WO 1998-EP1398 19980311. PRIORITY: DE 1997-19712718 19970326.

AB LHRH antagonists, esp. cetrorelix, are complexed with suitable biophilic carriers to enable sustained, targeted release of the active substance over a period of several weeks. The acidic polyamino acids, polyaspartic and polyglutamic acids, are selected for complexation with cetrorelix. The cetrorelix/polyamino acid complexes are produced from aq. solns. by combining the solns. and pptg. the complexes which are subsequently centrifuged off and vacuum dried over P2O5, preferably by lyophilization. These acidic polyamino acids display good sustained-release properties in a static liberation system depending on the hydrophobicity and molar mass of the polyamino acids. Animal testing demonstrated the efficacy of the cetrorelix/polyamino acid complexes as a depot system. By complexation of cetrorelix with polyamino acids, testosterone suppression can be achieved in male rats over a period of 600 h. Active substance release can thus be controlled according to polymer type and molar mass.

L94 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2001 ACS

1999:538778 Document No. 131:139954 LHRH antagonists in the treatment of **fertility** disorders. Bouchard, Philippe; Frydman, Rene; Diedrich, Klaus; **Engel, Jurgen;** Devroey, Paul (Asta Medica AG, Germany). Can. Pat. Appl. CA 2200541 AA 19980722, 15 pp. (English). CODEN: CPXXEB.

APPLICATION: CA 1997-2200541 19970320. PRIORITY: US 1997-786937 19970122.

AB A method of treating **infertility** disorders by administering an LH-RH antagonist, preferably Cetrorelix, in amts. to selectively suppress endogenous LH but not FSH secretion and inducing follicle growth by administration of exogenous gonadotropin. The selective suppression of LH allows FSH secretion to be at natural levels thereby not affecting individual estrogen development. The LH-RH antagonist can be given as a single or dual s.c. dose in the range of 1 mg to 10 mg, preferably 2 mg - 6 mg. In multiple dosing posol., LH-RH antagonist can be administered s.c. in an amt. in the range of 0.1 to 0.5 mg of LH-RH antagonist/day. LH-RH antagonist is applied starting cycle day 1 to 10, preferably on day 4 to 8, and ovulation can be induced between day 9 and 20 of the menstruation cycle by administering rec. LH, native LH-RH, LH-RH agonist or by HCG. In addn. rec. LH, native LH-RH or LH-RH agonist can be given to avoid hyperstimulation syndrome and native LH-RH or a LH-RH agonist can be administered to avoid luteal phase stimulation by neutralizing the neg. effects of HCG.

L94 ANSWER 7 OF 22 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1998-522092 [45] WPIDS

AB DE 19712718 A UPAB: 19981111

Complexes (I) of luteinising hormone releasing hormone (LHRH) antagonists (II) with polyaminoacids (III) (specifically polyglutamic acid or

polyaspartic acid) are new.

Also claimed are medicaments containing (I) (optionally together with conventional additives, structuring agents and stabilisers); and the production of an immobilised, activity-stabilised, parenterally administered peptide hormone preparation by precipitating (I) from aqueous solution.

USE - (I) are used for the treatment of hormone-sensitive tumours (especially mammary, ovarian or prostate carcinoma), benign prostate hypertrophy, **fertility** disorders or endometriosis; or in combination with hysteroscopy or in vitro **fertilisation** (all claimed).

ADVANTAGE - Complexation of the active agent (II) with the biophilic carrier (III) provides a stable retard/depot system for controlled release of (II) over several weeks. (II) is also protected against proteolytic degradation. (III) has a high binding affinity for (II).

Dwg.4/4

L94 ANSWER 8 OF 22 MEDLINE

1998344009 Document Number: 98344009. Impaired megakaryopoiesis and behavioral defects in mafG-null mutant mice. Shavit J A; Motohashi H; Onodera K; Akasaka J; Yamamoto M; **Engel J D.** (Department of Biochemistry, Molecular Biology, and Cell Biology, Northwestern University, Evanston, Illinois 60208-3500 USA.) GENES AND DEVELOPMENT, (1998 Jul 15) 12 (14) 2164-74. Journal code: FN3. ISSN: 0890-9369. Pub. country: United States. Language: English.

AB The small Maf proteins (MafG, MafK, and MafF), which serve as heterodimeric partner molecules of CNC family proteins for binding in vitro to MARE sites, have been implicated in the regulation of both transcription and chromatin structure, but there is no current evidence that the proteins fulfill these functions in vivo. To elucidate possible contributions of the small Maf proteins to gene regulation, we have ablated the mafG and mafK genes in mice by replacing their entire coding sequences with the Escherichia coli lacZ gene. mafG homozygous mutant animals exhibit impaired platelet formation accompanied by megakaryocyte proliferation, as well as behavioral abnormalities, whereas mafK-null mutant mice are phenotypically normal. Characterization of the mafG and mafK embryonic expression patterns show that their developmental programs are distinct and intersecting, but not entirely overlapping. These results provide direct evidence that the small Maf transcription factors are vital participants in embryonic development and cellular differentiation.

L94 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 4

1997:554033 Document No. 127:157215 LH-RH-antagonists in the treatment of **fertility** disorders. **Engel, Juergen Prof Dr**; Bouchard, Philippe Bouchard; Frydman, Rene Prof Dr; Diedrich, Klaus Prof Dr; Devroey, Paul Prof Dr (Asta Medica Aktiengesellschaft, Germany). Eur. Pat. Appl. EP 788799 A2 19970813, 4 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1997-100852 19970121. PRIORITY: US 1996-11282 19960207.

AB This invention relates to the prepn. of a medicament to be applied in the

field of treating **infertility** disorders with or without assisted reprodn. techniques. In particular the improvement is directed to use an LH-RH antagonist, preferably Cetrorelix, for prepn. of an medicament applied in the method of treating **infertility** disorders by inducing follicle growth by administration of exogenous gonadotropins and in administering the LH-RH antagonist which contains an amt. of LH-RH antagonist as low as only to suppress endogenous LH but the FSH secretion is maintained at a natural level and the individual estrogen development is not affected. When using the prepn., the follicle development must not be in each case externally stimulated (e.g. by the addn. of gonadotropins) but can be maintained by endogenous gonadotropins. Advantageously the prepn. can be given in the range of 0.1 to 5 mg of Cetrorelix/day during a multiple dosing posol.

L94 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2001 ACS
1998:29519 Document No. 128:162903 Antagonistic analogs of LHRH in oncology and gynecology. Schally, A. V.; Comaru-Schally, A. M.; Gonzalez-Barcena, D.; Reissmann, T.; **Engel, J.** (UK). Int. Congr., Symp. Semin. Ser., 13(Endometriosis Today), 401-413 (English) 1997. CODEN: ICGSEM. ISSN: 0969-2622. Publisher: Parthenon Publishing Group Ltd..
AB A review with 70 refs. LHRH antagonists, esp. cetrorelix, are reviewed along with their prospective clin. applicability to in vitro **fertilization**/embryo transfer, gynecol. oncol., fibroids, endometriosis and prostate disorders.

L94 ANSWER 11 OF 22 BIOSIS COPYRIGHT 2001 BIOSIS
1998:314838 Document No.: PREV199800314838. Studies on Geocalycaeae (Hepatiae). X. New taxa and new combinations in Chiloscyphus corda for Australasia. **Engel, John J. (1).** (1) Dep. Botany, Field Museum, Chicago, IL 60605-2496 USA. Phytologia, (July, 1997) Vol. 83, No. 1, pp. 42-46. ISSN: 0031-9430. Language: English.
AB Chiloscyphus subg. Lophocolea is a new combination. Chiloscyphus erosus, C. **fertilis**, C. subopposítus, C. edentatus, C. tuberculatus, C. connatifolius, C. parvispinus, C. semiteres var. retusus, C. mittenianus var. obtusus, and C. mittenianus var. symmetricus are described as new species and varieties from Australasia. Chiloscyphus subporosus var. inflexifolius is a new combination.

L94 ANSWER 12 OF 22 MEDLINE DUPLICATE 5
96077434 Document Number: 96077434. Development and applications of luteinizing hormone-releasing hormone antagonists in the treatment of **infertility**: an overview. Reissmann T; Felberbaum R; Diedrich K; **Engel J**; Comaru-Schally A M; Schally A V. (Clinic for Obstetrics and Gynaecology, University of Lubeck, Germany.) HUMAN REPRODUCTION, (1995 Aug) 10 (8) 1974-81. Ref: 62. Journal code: HRP. ISSN: 0268-1161. Pub. country: ENGLAND: United Kingdom. Language: English.
AB Luteinizing hormone-releasing hormone (LHRH) plays a crucial role in controlling the ovarian cycle in women. By modification of the molecular structure of this decapeptide, analogues were synthesized with agonistic or antagonistic effects on the gonadotrophic cells of the anterior pituitary gland. The agonists, after an initial stimulatory effect ('flare up'), lead to desensitization of the gonadotrophic cells and a reduction

in the number of LHRH receptors on the cell membrane ('down-regulation'), while the antagonists produce an immediate effect by competitive blockade of the LHRH receptors. After administration of LHRH antagonists, the serum levels of FSH and LH decrease within hours. Nevertheless, the adenohypophysis maintains its responsiveness to an LHRH stimulus ('pituitary response') after pretreatment with an antagonist. This different pharmacological mechanism of LHRH antagonists makes possible new approaches to ovarian stimulation and to the therapy of sex steroid dependent diseases. The premature LH surge, the main cause of cancellation during induction of superovulation in assisted reproduction technology (ART) programmes, can be abolished by short term application of an LHRH antagonist associated with a reduced human menopausal gonadotrophin (HMG) requirement for ovarian stimulation. A future approach to ART might be based on the combination of pretreatment with an LHRH antagonist and ovulation induction by native LHRH or an agonist. The severe side effects encountered with early LHRH antagonists, such as anaphylactoid reactions due to histamine release, are almost completely eliminated in modern antagonists, especially Cetrorelix which is presently used clinically in controlled phase II clinical studies.

L94 ANSWER 13 OF 22 MEDLINE DUPLICATE 6

96021031 Document Number: 96021031. Targeted disruption of the GATA3 gene causes severe abnormalities in the nervous system and in fetal liver haematopoiesis [see comments]. Pandolfi P P; Roth M E; Karis A; Leonard M W; Dzierzak E; Grosveld F G; **Engel J D**; Lindenbaum M H. (Dept. of Haematology, Royal Postgraduate Medical School, Hammersmith Hospital, London, UK.) NATURE GENETICS, (1995 Sep) 11 (1) 40-4. Journal code: BRO. ISSN: 1061-4036. Pub. country: United States. Language: English.

AB GATA-3 is one member of a growing family of related transcription factors which share a strongly conserved expression pattern in all vertebrate organisms. In order to elucidate GATA-3 function using a direct genetic approach, we have disrupted the murine gene by homologous recombination in embryonic stem cells. Mice heterozygous for the GATA3 mutation are **fertile** and appear in all respects to be normal, whereas homozygous mutant embryos die between days 11 and 12 postcoitum (p.c.) and display massive internal bleeding, marked growth retardation, severe deformities of the brain and spinal cord, and gross aberrations in fetal liver haematopoiesis.

L94 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 7

1994:587330 Document No. 121:187330 Preparation of a cetrorelix lyophilized composition. **Engel, Juergen**; Sauerbier, Dieter; Wichert, Burkhard; Reissmann, Thomas (Asta Medica AG, Germany). Eur. Pat. Appl. EP 611572 A2 19940824, 5 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE. (German). CODEN: EPXXDW. APPLICATION: EP 1994-101672 19940204. PRIORITY: DE 1993-4305225 19930219.

AB A lyophilizate of a peptide with 3-15 amino acid residues (e.g. cetrorelix) and .gtoreq.1 optional matrix materials (e.g. mannitol) is

prepd. by dissolving in 100-10,000 wt. parts AcOH, dilg. with water, and lyophilizing the resulting soln. The lyophilizate is useful for prepn. of

a medication for treatment of female **infertility** and protection of the gonads from the follicular hyperstimulation seen with other **infertility** treatments.

L94 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2001 ACS
1994:418062 Document No. 121:18062 Injection solutions containing mesna. **Engel, Juergen**; Wolf-Heuss, Elisabeth; Deger, Wolfgang; Camuglia, Giancarlo; Sauerbier, Dieter (ASTA Medica AG, Germany). Eur. Pat. Appl. EP 591710 A1 19940413, 6 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE. (German). CODEN: EPXXDW.

APPLICATION: EP 1993-114670 19930913. PRIORITY: DE 1992-4233842 19921008.

AB Injectable solns. of mesna, which protects the urinary tract from damage during antitumor treatment with oxazaphosphorines such as ifosfamide, are protected from microbial contamination with PhCH2OH at pH >7.5. Use of this high pH prevents deterioration owing to reaction of mesna with BzH (formed by oxidn. of PhCH2OH) to produce the thioacetal, PhCH(SCH2CH2SO3Na)2. Thus, an injection soln. contg. mesna 5000.0, PhCH2OH 520.0, and Na edetate 12.5 mg was adjusted to pH 8.0 with 10N NaOH, water was added to 50.0 mL, and the soln. was **sterilized** by filtration.

L94 ANSWER 16 OF 22 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
93024497 EMBASE Document No.: 1993024497. Modulation of the **fertilizing** ability of spermatozoa from roosters carrying the Sd (sperm degeneration) allele. Al-Aghbari A.; **Engel Jr. H.N.**; Froman D.P.. Department of Animal Sciences, Dryden Hall 208, Oregon State University,Corvallis, OR 97331-3402, United States. Biology of Reproduction 48/2 (308-312) 1993.
ISSN: 0006-3363. CODEN: BIREBV. Pub. Country: United States. Language: English. Summary Language: English.

AB Roosters carrying the Sd (sperm degeneration) allele produce spermatozoa that die prematurely in vivo. Consequently, these mutants are subfertile. The objective of the present study was to determine whether or not subfertility could be modulated. A previous study found that the proximal efferent ducts of mutants were characterized by a reduced surface-to-volume ratio. We hypothesized that if subfertility was exacerbated by hemicastration of chicks, which increases daily sperm production in adults, then a relationship between efferent duct function and sperm longevity would be likely. In experiment 1, hemicastration of chicks exacerbated the subfertility of adults ($p < 0.001$). As inferred from SDS-PAGE in previous research, mutants lack at least one non-albumin seminal plasma protein. Therefore, it was hypothesized that protein supplementation would ameliorate subfertility. In experiment 2, **fertility** increased ($p < 0.001$) when spermatozoa from mutants were mixed with albumin-depleted seminal plasma protein from **fertile** roosters before insemination. In contrast, supplementation with BSA had no

effect ($p > 0.05$). In summary, the subfertile status of Sd roosters was dynamic and appeared to depend upon the interaction of testicular output, efferent duct structure, and seminal plasma protein. Thus the study of this dysfunction may help to identify factors responsible for sperm

maturation in the domestic fowl.

L94 ANSWER 17 OF 22 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1992-150804 [18] WPIDS
AB WO 9206101 A UPAB: 19931006
Method comprises applying a solvent-free organoalkoxysilane liq. of formula (I) (R = 1-30C alkyl, cycloalkyl, arylalkyl and/or alkaryl, fully saturated with H or contg. double bonds or hetero-atoms, or their fluorinated derivs.; R' = 1-8C alkyl and/or alkoxyalkyl; n = 1-8); and allowing the organoalkoxysilane to cure.

An oleophobic organofluoro cpd. (esp. a fluoropolymer) may be mixed into the liq. and may include a volatile solvent which is removed prior to application.

USE/ADVANTAGE - In the protection of masonry prods., the repellents do not change the appearance of the substrate, are stable over a wide range of pH, are long wearing, and provide effective chloride ion screens.

Esp. they release low levels of volatile organics into the environment, and can be made oleophobic to produce a graffiti-resistant surface. (0/0)

0/0

ABEQ US 5112393 A UPAB: 19931006
Process for the removal of deleterious contaminants from a used electroless metal plating bath soln. contg. at least plating metal ions and Na-ions in sulphate form to recover the plating ions and permit reuse of the soln. at a selected pH, carried out by; (a) passing at least a portion of the used bath soln. through an acid cation exchanger from strong acid and intermediate-strong acid combination exchangers, in H-form, to remove the Na and plating metal ions by exchange with H-ions of the exchanger, and to convert sulphate, phosphites and non-sorbed constituents in the soln. to their respective acids in the exchanger effluent; (b) adding a basic Ca-salt to the exchanger effluent to ppte. calcium sulphate hemihydrate therefrom; (c) removing the pptd. calcium sulphate hemihydrate to produce a liq. phase; (d) recovering the liq. phase; (c) adding a basic Mg-salt to the liq. phase to ppte. magnesium phosphite tri-hydrate; (f) removing the pptd. magnesium phosphite tri-hydrate to produce a magnesium sulphate liq. phase; (g) recovering the magnesium sulphate liq. phase; and (h) eluting the plating metal ions from the cation exchanger.

USE/ADVANTAGE - The method can be used to recover valuable bath constituents e.g. plating metal, reducing agents, etc. which can be recycled to the bath. It can be used periodically or continuously on a side stream, to achieve bath purification, preventing plating operation degradation. The pptes. can be disposed of in a non-hazardous landfill or used in e.g. **fertilizer** prodn.

ABEQ EP 552149 A UPAB: 19931118
Method comprises applying a solvent-free organoalkoxysilane liq. of formula (I) (R = 1-30C alkyl,cycloalkyl, arylalkyl and/or alkaryl fully saturated with H or contg. double bonds of hetero-atoms, or their fluorinated devivs.; R' = 1-8C alkyl and/or alkoxyalkyl; n = 1-8); and allowing the organoalkoxysilane to cure. An oleophobic organofluoro cpd. (esp. a fluoropolymer) may be mixed into the liq. and may include a

volatile solvent which is removed prior to application.

USE/ADVANTAGE - In the protection of masonary prods., the repellents do not change the appearance of the substrate, are stable over a wide range of pH, are long wearing, and provide effective chloride ion screens.

Esp. they release low levels of volatile organics into the environment, and can be made oleophobic to produce a graffiti-resistant surface.

L94 ANSWER 18 OF 22 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

90107608 EMBASE Document No.: 1990107608. Decreased spermatozoal survivability associated with aberrant morphology of the ductili efferentes proximales of the chicken (Gallus domesticus). Kirby J.D.; Froman D.P.; **Engel Jr. H.N.**; Bernier P.E.; Hess R.A.. Department of Poultry Science, Oregon State University,Corvallis, OR 97331, United States. Biology of Reproduction 42/2 (383-389) 1990. ISSN: 0006-3363. CODEN: BIREBV. Pub. Country: United States. Language: English. Summary Language: English.

AB The objectives of this research were twofold: 1) to determine if decreased spermatozoal longevity, a previously reported heritable trait in chickens, was attributable to spermatozoal passage through the excurrent ducts, and 2) to document the morphology of the testicular excurrent ducts from affected roosters. Though spermatozoa were viable at ejaculation, as evidenced by their exclusion of ethidium bromide, **fertility** after intravaginal insemination of spermatozoa from affected roosters was less ($p<0.001$) than that observed with spermatozoa from nonaffected controls, 37 .+-. 2.3 versus 58 .+-. 1.5%, respectively, over a 21-day egg-collection interval. In contrast, **fertility** after intramagnal insemination of testicular spermatozoa from affected roosters was equivalent ($p>0.05$) to that of nonaffected controls, 47 .+-. 2.2 versus 41 .+-. 3.6%, respectively. After intravaginal insemination, neither type of testicular spermatozoa **fertilizaed** oocytes. The ductuli efferentes proximales from affected roosters were characterized by a greater luminal cross-sectional area as well as a diminished height and number of longitudinal epithelial folds ($p<0.005$). It was concluded that heritable decreased spermatozoal longevity in the chicken is not attributable to an inherent spermatozoal defect. Rather, the defect is acquired during passage of spermatozoa through the extragonadal ducts of the rooster.

L94 ANSWER 19 OF 22 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

89183432 EMBASE Document No.: 1989183432. Decreased sperm survivability in subfertile Delaware roosters as indicated by comparative and competitive **fertilization**. Kirby J.D.; Froman D.P.; **Engel Jr. H.N.**; Bernier P.E.. Department of Poultry Science, College of Veterinary Medicine, Oregon State University, Corvallis, OR 97331-3402, United States. Journal of Reproduction and Fertility 86/2 (671-677) 1989. ISSN: 0022-4251. CODEN: JRPFA4. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Duration of **fertility** following intravaginal and intramagnal insemination of hens with viable spermatozoa from subfertile Delaware roosters was compared with that obtained with spermatozoa from **fertile** Leghorns and subfertile Wyandotte roosters. In contrast to results with Leghorn and Wyandotte birds, duration of **fertility**

was not increased following intramagnal insemination of spermatozoa from Delaware birds. Competitive **fertilization** also demonstrated that duration of **fertility** was less than expected in the spermatozoa from Delaware birds. Heritable subfertility in Wyandotte and Delaware roosters therefore appears to be attributable to distinct sperm defects.

L94 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2001 ACS
1985:32242 Document No. 102:32242
(1,2-Diphenylethylenediamine)-platinum(II)
complex compounds. Schoenenberger, Helmut; Wappes, Beate; Jennerwein, Margaretha; Von Angerer, Erwin; **Engel, Juergen** (Degussa A.-G., Fed. Rep. Ger.). Ger. Offen. DE 3405611 A1 19840823, 43 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1984-3405611 19840216. PRIORITY: DE 1983-3305636 19830218.
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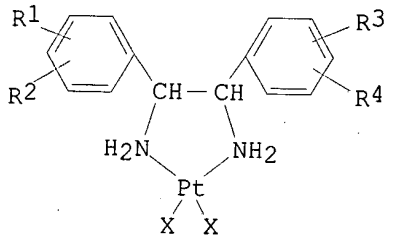

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AB The prepn. of antitumor pharmaceuticals contg. (1,2-diphenylethylenediamine) Pt(II)-complexes I (where R1, R2, R3, R4, same or different, are: H, OH, C1-6 alkoxy, substituted C2-6 alkanoyloxy or C3-6 alkenoxyloxy, of which at least one R group is not H; X = physiol. tolerable anion) is given. Thus, (+)-dichloro-[1,2-bis-(4-hydroxyphenyl)ethylenediamine]platinum(II) (II) [91326-62-4], dissolved in H2O with a pH of 2.5-3.5 after **sterilization** filtration, is an effective injectable soln. II was prepd. from K2PtCl4 and (+)-1,2-bis(4-hydroxyphenyl)ethylenediamine-2HBr [91548-22-0].

L94 ANSWER 21 OF 22 BIOSIS COPYRIGHT 2001 BIOSIS
1977:189745 Document No.: BA64:12109. YIELD LEAF GROWTH AND TILLERING IN BAHIA
GRASS BY NITROGEN RATE AND SEASON. BEATY E R; **ENGEL J L**; POWELL J D. AGRON J, (1977) 69 (2), 308-311. CODEN: AGJOAT. ISSN: 0002-1962. Language: Unavailable.
AB To test the concept that a yield predictive model could be developed, an established Pensacola bahiagrass (Paspalum notatum Flugge) sod was **fertilized** with 0, 84, 168 and 336 kg/ha N in 1973 and 1974. Starting in early June and continuing until Oct. plots were clipped monthly at heights of 2.5 and 7.5 cm. Before clipping, 10 tillers with mature leaves per plot were collected and numbers of clipped elongated and unclipped leaves were determined. Tillers on duplicate (15 cm)2 areas were

counted after clipping. Dry forage was increased over the 0 N check by adding 84 and 168 kg/ha N. The 336 kg/ha N did not increase forage yields over 168 kg/ha N. Clipping at 2.5 cm produced almost 3 times as much forate as clipping at 7.5 cm. Number of leaves per stolon per season averaged 20.2-22.0 and was influenced by N rate. At each of the 5 harvest dates, an average of 1.3 leaves/tiller (growing point) was elongating. N application increased tiller numbers by up to 300% and the largest number of new tillers occurred in June. Some data as collected were predictive of

N and leaf generation rate, but variations in tiller numbers per area and probably leaf weight per N relationships prevented the development of an effective yield prediction model. Further refinement of the data is needed. Statistical models based on tillers per area were not effective in

predicting yields. The lack of an effective relationship between tillers per area and yield was believed due to many young tillers dying before contributing to yield and variations in leaf size reflecting N **fertilization** and tiller age.

L94 ANSWER 22 OF 22 MEDLINE
73066031 Document Number: 73066031. Effects of tetrabenazine on lordosis behaviour and on brain monoamines in the female rat. Ahlenius S; **Engel J**; Eriksson H; Sodersten P. JOURNAL OF NEURAL TRANSMISSION, (1972) 33 (2) 155-62. Journal code: JAJ. ISSN: 0300-9564. Pub. country: Austria. Language: English.

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